PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

WEST-WALKER, Gregory, James
A J Park
6th Floor
Huddart Parker Building
1 Post Office Square, P.O. Box 949
Wellington 6015
NOUVELLE-ZÉLANDE

Date of mailing (day/month/year) 22 March 2001 (22.03.01)	
Applicant's or agent's file reference 25659 MRB	**IMPORTANT NOTIFICATION**
International application No. PCT/NZ00/00027	**International filing date** (day/month/year) 15 March 2000 (15.03.00)

1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

Name and Address	State of Nationality	State of Residence
BENNETT, Michael, Roy West-Walker Bennett Mobil on the Park 157 Lambton Quay Wellington New Zealand		
	Telephone No. 64 4 499 9058	
	Facsimile No. 64 4 499 9306	
	Teleprinter No.	

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☒ the name ☒ the address ☐ the nationality ☐ the residence

Name and Address	State of Nationality	State of Residence
WEST-WALKER, Gregory, James A J Park 6th Floor Huddart Parker Building 1 Post Office Square, P.O. Box 949 Wellington 6015 New Zealand		
	Telephone No. 64-4-473 8278	
	Facsimile No. 64-4-472 3358	
	Teleprinter No.	

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office
☐ the International Searching Authority
☐ the International Preliminary Examining Authority
☐ the designated Offices concerned
☒ the elected Offices concerned
☐ other:

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer J. Leitao
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year)	
20 October 2000 (20.10.00)	
International application No. PCT/NZ00/00027	**Applicant's or agent's file reference** 25659 MRB
International filing date (day/month/year) 15 March 2000 (15.03.00)	**Priority date** (day/month/year) 15 March 1999 (15.03.99)

Applicant

LE GROS, Graham, Stephen et al

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

09 October 2000 (09.10.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Manu Berrod
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PA[illegible]NT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

WEST-WALKER, Gregory, James
A J Park
6th Floor
Huddart Parker Building
1 Post Office Square, P.O. Box 949
Wellington 6015
NOUVELLE-ZÉLANDE

Date of mailing (day/month/year)
02 November 2001 (02.11.01)

Applicant's or agent's file reference
25659 MRB

IMPORTANT NOTIFICATION

International application No.
PCT/NZ00/00027

International filing date (day/month/year)
15 March 2000 (15.03.00)

RECEIVED
TECH CENTER 1600/2900
MAY 23 2002

1. The following indications appeared on record concerning:

[X] the applicant [ ] the inventor [ ] the agent [ ] the common representative

Name and Address

State of Nationality | State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[X] the person [X] the name [X] the address [X] the nationality [X] the residence

Name and Address

AGRESEARCH LIMITED
5th floor
Tower Block
Ruakura Reserach Centre
East Street
Hamilton
New Zealand

State of Nationality: NZ | State of Residence: NZ

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:
Additional applicant for all designated States except US.

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[ ] the designated Offices concerned
[X] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
François BAECHLER

Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994) 004424527

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
25659 MRB		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/NZ00/00027	15 March 2000	15 March 1999

Applicant

THE MALAGHAN INSTITUTE OF MEDICAL RESEARCH

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

   [ ] Contained in the international application in written form.

   [ ] Filed together with the international application in computer readable form.

   [ ] Furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readable form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [X] **Unity of invention is lacking** (See Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure

   [ ] because this figure better characterizes the invention

   [X] None of the figures

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ00/00027

A. CLASSIFICATION OF SUBJECT MATTER

Int. Cl. [7]: A61K 31/739

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS: Lipoarabinomannan, LAM, inhalant, airway, respiratory, aerosol, intranasal, asthma.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	LAWN, S.D. Frimpong, E.H. and Nyarka, E. Evaluation of a commercial immunodiagnostic kit incorporating lipoarabinomannan in the serodiagnosis of pulmonary tuberculosis in Ghana. Tropical Medicine and International Health. Volume 2, Number 10.Pages 978-981. October 1997.	
A	Erb, Klaus Josef, Holloway, John W., Sobeck, Alexandra, Moll, Heidrun and Le Gros, Graham. Infection of Mice with Mycobacterium bovis-Bacillus Calmette-Guérin (BCG) Suppresses Allergen-induced Airway Eosinophilia. Journal of Experimental Medicine. Volume 187, Number 4. 1998. 561-569	

☐ Further documents are listed in the continuation of Box C ☐ See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
20 July 2000	11 AUG 2000
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized officer A. WILCOX Telephone No : (02) 6283 2243

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ00/00027

Box I **Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)**

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos :

because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos :

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos :

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box II **Observations where unity of invention is lacking (Continuation of item 3 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Claims 1-31 are directed to an inhalant vaccine comprising Lipoarabinomannan for use in the treatment of asthma.
Claims 32-34 are directed to any inhalant dispensing device.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Claims 1-31.

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

PCT

INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
A61K 31/739

A1

(11) International Publication Number: WO 00/54783

(43) International Publication Date: 21 September 2000 (21.09.00)

(21) International Application Number: PCT/NZ00/00027

(22) International Filing Date: 15 March 2000 (15.03.00)

(30) Priority Data:
334664 15 March 1999 (15.03.99) NZ

(71) Applicants *(for all designated States except US)*: THE MALAGHAN INSTITUTE OF MEDICAL RESEARCH [NZ/NZ]; Mein Street, Newtown, Wellington (NZ). UNIVERSITY OF OTAGO [NZ/NZ]; Leith Street, Dunedin (NZ).

(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: LE GROS, Graham, Stephen [NZ/NZ]; 95 Ashton Fitchett Drive, Wellington (NZ). SCANGA, Connie, Black [US/NZ]; 16/20 Alpha Street, Te Aro, Wellington (NZ). BEASLEY, Charles, Richard, William [NZ/NZ]; 9 Wilton Road, Wellington (NZ). HARPER, Jacquie, Lucille [NZ/NZ]; 35 Maungaraki Road, Korokoro, Lower Hutt (NZ). SHIRTCLIFFE, Philippa [NZ/NZ]; 34 Calcutta Street, Khandallah, Wellington (NZ).

(74) Agents: BENNETT, Michael, Roy et al.; West-Walker Bennett, Mobil on the Park, 157 Lambton Quay, Wellington (NZ).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.
Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.

(54) Title: TREATMENT OF ASTHMA

(57) Abstract

The invention provides a respiratorially–administrable vaccine for use in treating asthma. The vaccines of the invention comprise lipoaribinomannan (LAM) in an immunogenic form.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	**ES**	Spain	**LS**	Lesotho	**SI**	Slovenia
AM	Armenia	**FI**	Finland	**LT**	Lithuania	**SK**	Slovakia
AT	Austria	**FR**	France	**LU**	Luxembourg	**SN**	Senegal
AU	Australia	**GA**	Gabon	**LV**	Latvia	**SZ**	Swaziland
AZ	Azerbaijan	**GB**	United Kingdom	**MC**	Monaco	**TD**	Chad
BA	Bosnia and Herzegovina	**GE**	Georgia	**MD**	Republic of Moldova	**TG**	Togo
BB	Barbados	**GH**	Ghana	**MG**	Madagascar	**TJ**	Tajikistan
BE	Belgium	**GN**	Guinea	**MK**	The former Yugoslav Republic of Macedonia	**TM**	Turkmenistan
BF	Burkina Faso	**GR**	Greece			**TR**	Turkey
BG	Bulgaria	**HU**	Hungary	**ML**	Mali	**TT**	Trinidad and Tobago
BJ	Benin	**IE**	Ireland	**MN**	Mongolia	**UA**	Ukraine
BR	Brazil	**IL**	Israel	**MR**	Mauritania	**UG**	Uganda
BY	Belarus	**IS**	Iceland	**MW**	Malawi	**US**	United States of America
CA	Canada	**IT**	Italy	**MX**	Mexico	**UZ**	Uzbekistan
CF	Central African Republic	**JP**	Japan	**NE**	Niger	**VN**	Viet Nam
CG	Congo	**KE**	Kenya	**NL**	Netherlands	**YU**	Yugoslavia
CH	Switzerland	**KG**	Kyrgyzstan	**NO**	Norway	**ZW**	Zimbabwe
CI	Côte d'Ivoire	**KP**	Democratic People's Republic of Korea	**NZ**	New Zealand		
CM	Cameroon			**PL**	Poland		
CN	China	**KR**	Republic of Korea	**PT**	Portugal		
CU	Cuba	**KZ**	Kazakstan	**RO**	Romania		
CZ	Czech Republic	**LC**	Saint Lucia	**RU**	Russian Federation		
DE	Germany	**LI**	Liechtenstein	**SD**	Sudan		
DK	Denmark	**LK**	Sri Lanka	**SE**	Sweden		
EE	Estonia	**LR**	Liberia	**SG**	Singapore		

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ _____

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only

Identification of IPEA	Date of receipt of DEMAND

Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION		Applicant's or agent's file reference: 25659 MRB
International application No.: PCT/NZ00/00027	International filing date *(day/month/year)*: 15 March 2000(15/3/00)	(Earliest) Priority date *(day/month/year)*: 15 March 1999(15/3/99)

Title of invention: TREATMENT OF ASTHMA

Box No. II APPLICANT(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

THE MALAGHAN INSTITUTE OF
MEDICAL RESEARCH
Mein Street
Newtown, Wellington
New Zealand

Telephone No.:

Facsimile No.:

Teleprinter No.:

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

UNIVERSITY OF OTAGO
Leith Street
Dunedin
New Zealand

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

LE GROS, Graham Stephen
95 Ashton Fitchett Drive
Wellington
New Zealand

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

[X] Further applicants are indicated on a continuation sheet.

Sheet No. 2

International application No.
PCT/NZ00/00027

Continuation of Box No. II APPLICANT(S)

If none of the following sub-boxes is used, this sheet should not be included in the demand.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

SCANGA, Connie Black
16/20 Alpha Street
Te Aro
Wellington
New Zealand

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
USA	New Zealand

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

BEASLEY, Charles Richard William
9 Wilton Road
Wellington
New Zealand

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
New Zealand	New Zealand

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

HARPER, Jacquie Lucille
35 Maungaraki Road
Korokoro
Lower Hutt
New Zealand

State *(that is, country)* of nationality:	State *(that is, country)* of residence:
New Zealand	New Zealand

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

State *(that is, country)* of nationality:	State *(that is, country)* of residence:

☐ Further applicants are indicated on another continuation sheet.

International application No.
PCT/NZ00/00027

Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The following person is [X] agent [ ] common representative

and [X] has been appointed earlier and represents the applicant(s) also for international preliminary examination.

[ ] is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.

[ ] is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

BENNETT, Michael Roy; RUTLEDGE, Sue Moira;
WEST-WALKER, Gregory James
of WEST-WALKER BENNETT
L24, Mobil on the Park
157 Lambton Quay
Wellington
NEW ZEALAND

Telephone No.: 64 4 499 9058

Facsimile No.: 64 4 499 9306

Teleprinter No.:

[ ] **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION

Statement concerning amendments:*

1. The applicant wishes the international preliminary examination **to start on the basis of:**

[X] the international application as originally filed

the description [X] as originally filed
[ ] as amended under Article 34

the claims [X] as originally filed
[ ] as amended under Article 19 (together with any accompanying statement)
[ ] as amended under Article 34

the drawings [X] as originally filed
[ ] as amended under Article 34

2. [ ] The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

3. [ ] The applicant wishes the start of the international preliminary examination **to be postponed** until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: English

[X] which is the language in which the international application was filed.
[ ] which is the language of a translation furnished for the purposes of international search.
[ ] which is the language of publication of the international application.
[ ] which is the language of the translation (to be) furnished for the purposes of international preliminary examination.

Box No. V ELECTION OF STATES

The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

Sheet No. 4

International application No.
PCT/NZ00/00027

Box No. VI CHECK LIST

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:			For International Preliminary Examining Authority use only: received	not received
1. translation of international application	:	sheets	☐	☐
2. amendments under Article 34	:	sheets	☐	☐
3. copy (or, where required, translation) of amendments under Article 19	:	sheets	☐	☐
4. copy (or, where required, translation) of statement under Article 19	:	sheets	☐	☐
5. letter	:	sheets	☐	☐
6. other *(specify)*	:	sheets	☐	☐

The demand is also accompanied by the item(s) marked below:

1. [X] fee calculation sheet
2. [ ] separate signed power of attorney
3. [ ] copy of general power of attorney; reference number, if any:
4. [ ] statement explaining lack of signature
5. [ ] nucleotide and or amino acid sequence listing in computer readable form
6. [ ] other *(specify)*:

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

MICHAEL ROY BENNETT
Agent for the Applicants

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:
2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):
3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply. ☐ The applicant has been informed accordingly.
4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.
5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

CHAPTER II

PCT

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

International application No. PCT/NZ00/00027	For International Preliminary Examining Authority use only
Applicant's or agent's file reference 25659 MRB	Date stamp of the IPEA

Applicant THE MALAGHAN INSTITUTE OF MEDICAL RESEARCH and UNIVERSITY OF OTAGO

Calculation of prescribed fees

1. Preliminary examination fee	AUD450.00 P	
2. Handling fee *(Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.)*	AUD238.00 H	
3. Total of prescribed fees Add the amounts entered at P and H and enter total in the TOTAL box	AUD688.00 TOTAL	

Mode of Payment

☐	authorization to charge deposit account with the IPEA (see below)	☐	cash
☐	cheque	☐	revenue stamps
☐	postal money order	☐	coupons
☒	bank draft	☐	other *(specify)*:

Deposit Account Authorization *(this mode of payment may not be available at all IPEAs)*

The IPEA/ _____ ☐ is hereby authorized to charge the total fees indicated above to my deposit account.

☐ *(this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

Deposit Account Number _____ Date *(day/month/year)* _____ Signature _____

See Notes to the fee calculation sheet

ENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 25659 MRB	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. **PCT/NZ00/00027**	International Filing Date *(day/month/year)* 15 March 2000	Priority Date *(day/month/year)* 15 March 1999
International Patent Classification (IPC) or national classification and IPC **Int. Cl.** [7] A61K 31/739, A61P 11/06		
Applicant THE MALAGHAN INSTITUTE OF MEDICAL RESEARCH et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 3 sheets, including this cover sheet.

☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheet(s).

3. This report contains indications relating to the following items:

I	☒	Basis of the report
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

Date of submission of the demand	Date of completion of the report
9 October 2000	7 February 2001
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer **G.J. McNEICE** Telephone No. (02) 6283 2055

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*

Regional Patent

- [X] AP **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- [X] EA **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- [X] EP **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- [X] OA **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

- [X] AE United Arab Emirates
- [X] AL Albania
- [X] AM Armenia
- [X] AT Austria
- [X] AU Australia
- [X] AZ Azerbaijan
- [X] BA Bosnia and Herzegovina
- [X] BB Barbados
- [X] BG Bulgaria
- [X] BR Brazil
- [X] BY Belarus
- [X] CA Canada
- [X] CH and LI Switzerland and Liechtenstein
- [X] CN China
- [X] CR Costa Rica
- [X] CU Cuba
- [X] CZ Czech Republic
- [X] DE Germany
- [X] DK Denmark
- [X] DM Dominica
- [X] EE Estonia
- [X] ES Spain
- [X] FI Finland
- [X] GB United Kingdom
- [X] GD Grenada
- [X] GE Georgia
- [X] GH Ghana
- [X] GM Gambia
- [X] HR Croatia
- [X] HU Hungary
- [X] ID Indonesia
- [X] IL Israel
- [X] IN India
- [X] IS Iceland
- [X] JP Japan
- [X] KE Kenya
- [X] KG Kyrgyzstan
- [X] KP Democratic People's Republic of Korea
- [X] KR Republic of Korea
- [X] KZ Kazakhstan
- [X] LC Saint Lucia
- [X] LK Sri Lanka
- [X] LR Liberia
- [X] LS Lesotho
- [X] LT Lithuania
- [X] LU Luxembourg
- [X] LV Latvia
- [X] MA Morocco
- [X] MD Republic of Moldova
- [X] MG Madagascar
- [X] MK The former Yugoslav Republic of Macedonia
- [X] MN Mongolia
- [X] MW Malawi
- [X] MX Mexico
- [X] NO Norway
- [X] NZ New Zealand
- [X] PL Poland
- [X] PT Portugal
- [X] RO Romania
- [X] RU Russian Federation
- [X] SD Sudan
- [X] SE Sweden
- [X] SG Singapore
- [X] SI Slovenia
- [X] SK Slovakia
- [X] SL Sierra Leone
- [X] TJ Tajikistan
- [X] TM Turkmenistan
- [X] TR Turkey
- [X] TT Trinidad and Tobago
- [X] TZ United Republic of Tanzania
- [X] UA Ukraine
- [X] UG Uganda
- [X] US United States of America
- [X] UZ Uzbekistan
- [X] VN Viet Nam
- [X] YU Yugoslavia
- [X] ZA South Africa
- [X] ZW Zimbabwe

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

- [X] DZ. Algeria
- [ ]

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

Box No. VI PRIORITY CLAIM ☐ Further priority claims indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 15 March 1999 (15/3/1999)	NZ 334664	New Zealand		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): (1)

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used)*:

ISA / AU

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority)*:

Date *(day/month/year)* Number Country *(or regional Office)*

–

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request	:	5
description (excluding sequence listing part)	:	14
claims	:	4
abstract	:	1
drawings	:	5
sequence listing part of description	:	–
Total number of sheets	:	29

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☐ other *(specify)*:

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

MICHAEL ROY BENNETT
Agent for the Applicants

For receiving Office use only

1. Date of actual receipt of the purported international application:
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA /
6. ☐ Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

This sheet is not part of and does not count as a sheet of the international application.

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference: 25659 MRB

Applicant: THE MALAGHAN INSTITUTE OF MEDICAL RESEARCH and UNIVERSITY OF OTAGO

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . $180.00 [T]
2. SEARCH FEE . . . . . $990.00 [S]

International search to be carried out by Australian Patent Office

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 29 sheets.

first 30 sheets . . . . . $822.00 [b1]

_____ (remaining sheets) x _____ (additional amount) = – [b2]

Add amounts entered at b1 and b2 and enter total at B . . . . $822.00 [B]

Designation Fees

The international application contains 107 designations.

107 (number of designation fees payable *(maximum 8)*) x $178 (amount of designation fee) = $1424.00 [D]

Add amounts entered at B and D and enter total at I . . . . . $2246.00 [I]

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT *(if applicable)* . . . . . – [P]

5. TOTAL FEES PAYABLE . . . . . $3416.00 TOTAL

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

[X] The designation fees are not paid at this time.

MODE OF PAYMENT

- [ ] authorization to charge deposit account (see below)
- [ ] bank draft
- [ ] coupons
- [ ] cheque
- [ ] cash
- [ ] other *(specify):*
- [ ] postal money order
- [ ] revenue stamps

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/ _____

- [ ] is hereby authorized to charge the total fees indicated above to my deposit account.
- [ ] *(this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.
- [ ] is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

Deposit Account No. _____ Date *(day/month/year)* _____ Signature _____

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SHIRTCLIFFE, Philippa
34 Calcutta Street
Khandallah
Wellington
New Zealand

This person is:

- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

This person is applicant for the purposes of: [ ] all designated States [ ] all designated States except the United States of America [X] the United States of America only [ ] the States indicated in the Supplemental Box

---

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:

- [ ] applicant only
- [ ] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: [ ] all designated States [ ] all designated States except the United States of America [ ] the United States of America only [ ] the States indicated in the Supplemental Box

---

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:

- [ ] applicant only
- [ ] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: [ ] all designated States [ ] all designated States except the United States of America [ ] the United States of America only [ ] the States indicated in the Supplemental Box

---

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:

- [ ] applicant only
- [ ] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: [ ] all designated States [ ] all designated States except the United States of America [ ] the United States of America only [ ] the States indicated in the Supplemental Box

---

[ ] Further applicants and/or (further) inventors are indicated on another continuation sheet.

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

LE GROS, Graham Stephen
95 Ashton Fitchett Drive
Wellington
New Zealand

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

SCANGA, Connie Black
16/20 Alpha Street
Te Aro
Wellington
New Zealand

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: USA

State *(that is, country)* of residence: New Zealand

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

BEASLEY, Charles Richard William
9 Wilton Road
Wellington
New Zealand

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

HARPER, Jacquie Lucille
35 Maungaraki Road
Korokoro
Lower Hutt
New Zealand

This person is:
- [ ] applicant only
- [X] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [X] the United States of America only
- [ ] the States indicated in the Supplemental Box

[X] Further applicants and/or (further) inventors are indicated on another continuation sheet.

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* 25659 MRB

Box No. I TITLE OF INVENTION

TREATMENT OF ASTHMA

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

THE MALAGHAN INSTITUTE OF MEDICAL RESEARCH
Mein Street
Newtown
Wellington
New Zealand

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

UNIVERSITY OF OTAGO
Leith Street
Dunedin
New Zealand

This person is:

☒ applicant only

☐ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: New Zealand

State *(that is, country)* of residence: New Zealand

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

BENNETT, Michael Roy; WEST-WALKER, Gregory James;
RUTLEDGE, Sue Moira
of WEST-WALKER BENNETT
Mobil on the Park
157 Lambton Quay
Wellington
New Zealand

Telephone No. +64 4 499 9058

Facsimile No. +64 4 499 9306

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **1-34**	**YES**
	Claims	**NO**
Inventive step (IS)	Claims **1-34**	**YES**
	Claims	**NO**
Industrial applicability (IA)	Claims **1-34**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

Novelty (N) and Inventive Step(IS)

The citations in the International Search Report, namely

(i) Lawn, S.D.et al "Evaluation of a commercial immunodiagnostic kit including lipoarabinomannan in the serodiagnosis of pulmonary tuberculosis in Ghana." Tropical Medicine and International Health, Vol. 2, No. 10, Oct 1997, pages 978-981 and

(ii) Erb, K.J. et al, "Infection of Mice with Mycobacterium bovis - Bacillus Clamette-Guerin (BCG) suppresses allergen-induced airway eosinophilia." J. of Experimental Medicine, Vol. 187, No. 4, 1998, pages 561-569

do not disclose the lipoarabinomannan vaccine formulated for respiratory administration.

In Erb, Mycobacterium bovis is disclosed for treating asthma. Although Mycobacterium bovis produces lipoarabinomannan (see Lawn S.D. page 979, lines 4 to 5.), there would appear to be an inventive step in formulating a vaccine using this component.

Industrial Applicability (IA)

Industrial Applicability is not in doubt.

Rule 67 lists the subject matter which under Article 34(4)(a)(i) an international preliminary examination is not required to be carried out. At item (iv) it specifies methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods, as such matter. However the agreement between WIPO and Australia further qualifies this by excepting from exclusion any subject matter which is examined under national grant procedures. Claims 16-21 have nonetheless been considered because the identified subject matter does not contravene Australian law.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/NZ00/00027

I. Basis of the report

1. With regard to the **elements** of the international application:*

- [X] the international application as originally filed.
- [ ] the description, pages , as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the claims, pages , as originally filed,
  pages , as amended (together with any statement) under Article 19,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the drawings, pages , as originally filed,
  pages , filed with the demand,
  pages , received on with the letter of
- [ ] the sequence listing part of the description:
  pages , as originally filed
  pages , filed with the demand
  pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

- [ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- [ ] the language of publication of the international application (under Rule 48.3(b)).
- [ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, was on the basis of the sequence listing:

- [ ] contained in the international application in written form.
- [ ] filed together with the international application in computer readable form.
- [ ] furnished subsequently to this Authority in written form.
- [ ] furnished subsequently to this Authority in computer readable form.
- [ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- [ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:
   - [ ] the description, pages
   - [ ] the claims, Nos.
   - [ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

TREATMENT OF ASTHMA

This invention relates to the treatment of asthma. More particularly, it relates to both therapeutic treatment of asthma sufferers and to preventative (prophylactic) treatment of non-asthmatics against asthma.

BACKGROUND ART

Asthma is a chronic inflammatory disorder of the airways in which many cells play a role, including mast cells and eosinophils. In susceptible individuals this inflammation causes symptoms which are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment, and causes an associated increase in airway responsiveness to a variety of stimuli.

Asthma can be inherited, is not contagious and may be chronic and persistent or occurring in the form of attacks which are periodic and usually at least partly reversible. Attacks vary in severity and frequency from person to person. Many factors may contribute to the development of asthma including exposure to inhaled allergens such as pollens, mold spores, house dust mites and animal dander. In an individual who has developed asthma, many stimuli can trigger asthma attacks including allergens, viral respiratory infections (colds or the flu), irritants in the air (smoke, air pollution, perfume), damp, cold weather, and exercise.

During an asthma attack, the muscles around the bronchial tubes tighten and the linings of the bronchial tubes swell (become inflamed) and produce thick mucus, thereby decreasing the internal diameter of the tubes. These changes increase resistance to the flow of air making it hard to breathe. When asthma is properly controlled the bronchial tubes are of normal size.

Asthma is a common disease among both children and adults. An estimated 7% of people in the United States have been diagnosed as asthmatic. The corresponding figure for New Zealand is about 10% (Burney, P. *et al.* (1996) Variations in the Prevalence of Respiratory Symptoms, Self-Reported Asthma Attacks, and Use of Asthma Medication in the European Community Respiratory Health Survey. *Eur. Respir. J.* 9:687-695). The occurrence of asthma in both Western and developing

countries has increased markedly over the last 30 years. This relatively short time frame suggests that environmental rather than genetic factors are at work.

In most cases asthma is an atopic disorder in which the underlying process is due to an allergic response to common environmental allergens. This allergic response is a function of the immune system characterised by activation and recruitment of eosinophils to the lung causing the characteristic chronic swelling and inflammation of the airways that affects the breathing of sufferers.

The pharmaceutical treatment of asthma includes several different classes of drugs, including beta agonists, topical or oral steroids and theophyllines. If used appropriately, such treatments may keep asthma systems from developing or relieve them when they are present. Beta agonists and theophyllines primarily act by relaxing the muscles surrounding the airways while steroids act to reduce (and even prevent) inflammation and mucus production. Other medications exist and more are being developed due to the growing interest in and concern over the prevalence, morbidity and mortality of asthma world-wide.

There is an immunological basis to the development of airways inflammation in asthma, involving the Th2 lymphocytes (Th2s). These cells secrete cytokines, including interleukin-4 (IL-4) and IL-5, leading to enhanced production of immunoglobulin E (IgE) by B cells and the generation and recruitment of eosinophils respectively. Activation of mast cells by allergens releases histamine and other mediating chemicals that trigger an acute inflammatory response, including mucus production. Eosinophils release mediators including cytotoxins which lead to inflammation and necrosis of the bronchial epithelium. The localised recruitment and activation of eosinophils together with the resultant tissue damage is termed "eosinophilia".

A need therefore exists for an asthma treatment that modulates the immune system to reduce the risk of developing atopy and airways inflammation, in addition to the traditional treatment with drugs which suppress airways inflammation once it has already occurred, or drugs which reduce symptoms in an asthmatic individual. An added benefit would be if such a treatment also has a similar inhibitory effect in a current sufferer of an atopic disorder to reduce the severity of their disease.

One immunological approach to meet this need involves *Mycobacterium bovis - Bacillus Calmette-Guerin* (BCG). Prior active infection with this organism has been reported by Erb *et al* (*J. Exp. Med.*, Vol. 187, No. 4, February 16 1998) to suppress subsequent allergen-induced airway eosinophilia in mice, with intranasal infection being reported to be more effective than intraperitoneal or subcutaneous infection.

BCG as an organism and as BCG-Polysaccharide Nucleic Acid has also been reported as being used in the treatment of asthma in China (see, for example, *China J. Paedia* (1991); 39(3): 165-167, *Guangzhou Medical Journal* 1984; 15(2):16-18) and *Acta of Hu-Nan Medical University* 1992; 17:365-367. Intact BCG is reported as being administered both alive and dead. The reported routes of administration vary between intramuscular injection and scratch vaccination.

The present invention is directed to an alternative immunological approach involving, as active agent, a type of lipopolysaccharide in immunogenic form. The lipopolysaccharide is lipoaribinomannan (LAM).

Lipopolysaccharides (including LAM) have been included in immunological compositions previously. For example, US Patent specification 5,853,737 (Modlin) discusses various methods of inducing a CD1 restricted immune response and teaches of a vaccine containing CD1-presented non-polypeptide hydrophobic antigens and in particular a lipoarabinomannan (LAM) antigen.

Both US Patent specifications 4,329,452 and 4,394,502 (Maruyama) teach of the use of lipopolysaccharide as an active component in an immunotherapeutic agent for tumours. The lipopolysaccharide can be derived from human tubercle bacillus.

However, to the applicant's knowledge, LAM has not been employed as an immunoactive agent in a vaccine for treating asthma, either prophylactically or therapeutically, where the vaccine is administered to the airways of a patient.

It is therefore an object of this invention to provide an immunological approach to the treatment of asthma, both prophylactically (in relation to non-asthmatics) and therapeutically (in relation to asthmatics) which at least provides a useful choice over existing approaches.

SUMMARY OF THE INVENTION

In a first aspect, the invention provides a vaccine for inducing an immune response in a patient effective in the prophylactic treatment against, or therapeutic treatment of, asthma which comprises, as active agent, immunogenic lipoarabinomannan (LAM) formulated for respiratory administration to said patient.

As used herein, "immunogenic LAM" means LAM other than as part of an intact mycobacterial organism, which LAM is capable of inducing an immune response in a patient.

Preferably, said immunogenic LAM is substantially free of bacterial nucleic acid.

As used herein, "prophylactic treatment against asthma" means treatment of a non-asthmatic patient to prevent or at least reduce the likelihood of the patient becoming asthmatic.

As used herein, "therapeutic treatment of asthma" encompasses preventing, or reducing the severity of the symptoms of an asthmatic episode in an asthmatic patient, inclusive of bronchial inflammation and eosinophilia.

As used herein, "respiratory administration" means administration to the airways of a patient, including administration intranasally and by inhalation through the mouth to reach the respiratory tract.

The immune response induced is a non-CD1 restricted immune response.

The invention further provides a vaccine for reducing the severity of asthma comprising an immunologically effective amount of immunogenic LAM formulated for respiratory administration.

Still further, the invention provides a vaccine for reducing the risk of developing asthma comprising an immunologically effective amount of immunogenic LAM formulated for respiratory administration.

Conveniently, said immunogenic LAM is isolated from a mycobacterium, more c nveniently isolated from an *M. bovis* organism and most conveniently is isolated from *M. bovis* strain AN5.

Preferably, said LAM contains, as its saccharide component, from 27% to 52% mannose and from 73% to 48% arabinose, more preferably, from 40% to 50% mannose and from 60% to 50% arabinose, and most preferably approximately 45% mannose and approximately 55% arabinose.

It will be usual for said immunogenic LAM to be a fluid, and preferably in the form of a solution or suspension.

Conveniently, the vaccine will further comprise a respiratorially acceptable adjuvant, which may include a detergent or surfactant component.

A secondary immunogen selected from one or more Th1 type immune response inducing substances may also be present. Preferably, *Mycobacterium bovis* (Bacillus Calmette-Guerin) is included as said Th1 type immune response inducing substance.

In another aspect, the invention provides a method of prophylactically treating a non-asthmatic patient against asthma which comprises the step of inducing an immune response in said patient by respiratorially administering an effective amount of immunogenic LAM.

In yet another aspect, the invention provides a method of therapeutically treating asthma in a patient which comprises the step of inducing an immune response in said patient by respiratorially administering an effective amount of immunogenic LAM.

Again, the immune response induced is not a CD1 restricted immune response.

Conveniently, said immunogenic LAM is administered in the form of a vaccine as described above.

Usually, the immunogenic LAM will be administered by inhalation through the mouth or intranasally to said patient.

In yet another aspect, the invention provides the use of immunogenic LAM in the preparation of a medicament for the therapeutic treatment of asthma.

In still another aspect, the invention provides the use of immunogenic LAM in the preparation of a medicament for prophylactic treatment of a non-asthmatic against developing asthma.

In preferred embodiments, the immunogenic LAM is isolated from a mycobacterium, more preferably an *M. bovis* organism, and most preferably *M. bovis* strain AN5.

It is further preferred that the immunogenic LAM contains, as its saccharide component, from 27% to 52% mannose and from 73% to 48% arabinose, more preferably from 40% to 50% mannose and from 60% to 50% arabinose and most preferably approximately 45% mannose and approximately 55% arabinose.

It will be usual in preparing said medicament that said immunogenic LAM be combined with a respiratorially acceptable adjuvant such that the medicament is formulated for respiratory administration.

In a final aspect, the invention provides a device for prophylactically or therapeutically treating asthma which includes a container from which a vaccine as described above can be dispensed to the airways of a patient in need of such treatment.

The device will conveniently be one from which said vaccine is dispensable for inhalation through the mouth of a patient, or intranasally dispensable.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a graph showing number of cells recovered per ml of bronchoalveolar lavage (BAL) exudate.

Figure 2 is a graph showing total number of cells recovered by BAL.

Figure 3 is a graph showing the percentage of eosinophils recovered by BAL.

Figure 4 is a graph showing the percentage of macrophages recovered by BAL.

Figure 5 is a graph showing number of eosinophils recovered per ml of BAL exudate.

Figure 6 is a graph showing total number of eosinophils recovered by BAL.

Figure 7 is a graph showing the dose response curve for LAM as determined by numbers of eosinophils recovered per ml of BAL exudate.

Figure 8 is a graph showing the effect of LAM in CD1 Knock Out mice as determined by the number of eosinophils recovered per ml of BAL exudate.

BEST MODE OF PERFORMING THE INVENTION

As broadly outlined above, the present invention offers an approach to reducing the severity of airway eosinophilia and thus asthma in an asthmatic and/or for reducing the risk of developing airway eosinophilia and thus asthma in a non-asthmatic by introducing to the airways biologically active amounts of lipoarabinomannan (LAM) in an immunogenic form.

LAM is present in actinomycetes, which are a distinctive lineage of Gram-positive bacteria. Members of this lineage include *Rhodococcus equi, Corynebacterium diphtheriae, Corynebacterium matruchotii, Gordona rubropertincta, Gordona terrae, Rhodococcus rhodnii* and *Tsukamurella paurometabolum.*

Other members of the lineage include mycobacteria, with LAM being a major lipoglycan of the mycobacterial cell wall.

For use in the present invention, LAM can therefore be obtained by isolation from any suitable actinomycetes organism. It is however preferred that the immunogenic LAM for use in the invention be obtained from mycobacteria, particularly pathogenic mycobacteria, or from attenuated strains of pathogenic mycobacteria. However, LAM from non-pathogenic avirulent mycobacteria is by no means excluded.

The preference for pathogenic mycobacteria as a source for immunogen LAM arises from the association between LAM, mycobacterial pathogenesis and the ability of LAM t modulate Tumour Necrosis Factor-alpha (TNF-α) production (see the article "Relationships Between the Structure and the Roles of Lipoaribinomannans and Related Glycoconjugates", Vercellone *et al.*, *Frontiers in BioScience* 3, p 149-163 (1988)).

Particularly suitable mycobacteria from which LAM can be obtained are therefore *M. bovis*, *M. tuberculosis*, *M. vaccae* and *M. paratuberculosis*, with *M. bovis* organisms such as *M. bovis* strain AN5 being presently preferred.

The LAM can be isolated from such bacteria, and in particular from mycobacteria, using techniques which are standard in the art. By way of example, the procedure of Severn *et al.*, *J. Microb. Methods*, 28, 123-30 (1997) can be employed.

Isolated LAM will conveniently be purified for use in the present invention. The effect of this will be to exclude other bacterial components (including bacterial nucleic acid) from the LAM. Again, art standard techniques can be employed such as those described by Severn *et al.*

The saccharide composition of the immunogenic LAM can vary. Generally, any lipoglycan with a saccharide component containing both arabinose and mannose (and therefore qualifying as a LAM) can be used. However, it is preferred for there to be at least 27% of mannose present, with a preferred saccharide composition varying from 27% to 52% mannose and 73% to 48% arabinose.

More commonly, the saccharide component will include 40% to 50% mannose and 60% to 50% arabinose, with one particularly preferred LAM having a saccharide component which is approximately 45% mannose and 55% arabinose.

Once the LAM is obtained and preferably purified, it is formulated for respiratory administration. Respiratory administration requires delivery of the LAM to the airways of the patient to be treated. Generally, this will involve delivery through the mouth or intranasally. Often, inhalation by the patient will provide the motive force to the LAM. However, respiratory administration can also involve delivery by

propellant, including in the form of an aerosol generated using a jet or ultrasonic nebuliser. This is presently preferred.

For such applications, the LAM will conventionally be in a fluid form. This can be as a powder or as a solution or suspension (particularly for aerosol application).

The LAM will generally also be formulated for respiratory administration together with a respiratorially acceptable adjuvant. The selection of the adjuvant will be dependent upon the formulation and mode of dispensing involved, but will in any case be a matter of routine choice for the skilled worker in this field.

Where, as is preferred, the LAM is to be administered via a nebuliser-generated aerosol, the LAM will be in the form of a solution or suspension which will contain such adjuvant components. One such optional but preferred component is a non-toxic detergent or surfactant. Examples include a Polysorbate 80, beractant (Survanta Susp (Abbott)) and colfosceril palmitate (Exosurf Neonatal (Glaxo Wellcome)).

It is also possible to include an additional immunogen in the solution or suspension for administration as an aerosol. Such an immunogen will generally be a Th1 type immune response inducing substance. One such substance which can be included is BCG, alive or dead, but with dead being preferred.

Where BCG is included as a secondary immunogen, it will be usual for the solution or suspension to further comprise a non-clumping agent (such as Bovine Serum Albumin) to prevent the organisms from adhering together.

Despite the preference for aerosol administration, it is by no means intended to exclude administration of LAM in other forms. To the contrary, the LAM vaccine can be formulated for administration as a powder, for example using lactose capsules as a delivery vehicle in a dry powder inhaler.

The invention will now be exemplified through reference to the following experimental section, which it will be appreciated is illustrative and not limiting.

EXPERIMENTAL

SECTION A

LAM Isolation

Isolation of LAM from *M. bovis*

LAM was isolated and analysed by the procedures of Severn *et al.*, *J. Microb. Methods*, 28, 123-30 (1997) as described briefly below.

M. bovis strain AN5 (obtained from Central Veterinary Laboratories, Weybridge, UK) was grown as pellicles on modified Reid's synthetic medium. The cells were killed by heating at 100°C for 3 hours, washed with buffered saline and recovered by centrifugation. The cells were slurried in TBS, cooled and extruded by passing though a French pass. The disrupted cells were digested with RNAse (Boehringer Mannheim) and DNAse (Boehringer Mannheim) at 37°C and then 60°C.

Triton X-114 solution was added to the lysed cells, cooled on ice and stirred for 16 hours at 4°C. The cellular debris was removed by centrifugation and the supernatant was incubated at 37°C to induce phase separation. The lipoglycans were recovered from the lower Triton X-114 phase following precipitation by the addition of ethanol and centrifugation. The extract was further purified by treatment with Proteinase K and isolated by ultra-centrifugation. The lipoglycans were resolved into their separate species by size exclusion chromatography on Sephacryl s-200. Fractions containing LAM were identified using SDS-PAGE analysis.

Analysis of lipopolysaccharide

The purity of the combined LAM fractions was investigated. LAM was deemed pure based on the following criteria: 0% protein as indicated by the BCA protein assay performed as described by Severn *et al* (1997), absence of nitrogen as indicated by elemental analysis of the purified extracts, and the absence of ribose or deoxyribose in the glycose analysis (Severn *et al* (1997)).

The purified LAM was hydrolysed and acetylated (as described by Severn *et al* (1997)) and the resulting mixture of saccharides analysed by GLC as described by Severn *et*

al (1997)). The mixture was comprised of 45% mannose and 55% arabinose confirming that the saccharide component of the lipoglycan is arabomannin.

SECTION B

Formulation of LAM for respiratory administration

LAM, purified as in Section A, was formulated for intranasal administration in Phosphate Buffered Saline (PBS).

SECTION C

Efficacy of LAM

SECTION C1

Materials and Methods

An ovalbumin (OVA) induced airway eosinophilia mouse model of atopic airway inflammation was used to determine the effectiveness of the immunogenic LAM suppressing the development of airway eosinophilia. This model is widely used to establish "asthma-like effects" in mice - see for example, Erb *et al.*, *J. Exp. Med.* 187(4):561-569 (1998); Herz *et al.*, *J.Allergy and Clinical Immunology*, 102:867-874 (1998); and Randaolf *et al.*, *J. Clinical Investigation*, 104:1021-1029 (1999).

Briefly, antigen specific Th2 cells were primed to OVA in test mice by two successive intraperitoneal immunisations 14 days apart with OVA and by administration of an intranasal challenge of OVA 14 days after the second intraperitoneal immunisation.

To test efficacy of LAM, biologically active amounts of LAM in PBS were given intranasally to 5 primed mice 7 days after the second intraperitoneal immunisation. PBS was also administered intranasally to 5 primed mice as a control. 4 days post intranasal challenge bronchoalveolar lavage (BAL) was used to determine the degree of eosinophil inflammatory response in all mice. BAL exudates were examined for the presence of eosinophils.

BCG, alive or killed by heating at 56°C for 30 minutes, were given to groups of 5 mice at doses of $2x10^6$ colony forming unit (CFU) equivalents for comparison purposes. The doses were administered intranasally and their effect determined by BAL as described above.

In each case, PBS was administered intranasally to 5 primed mice as a control.

3 dosages of LAM in PBS were administered to the airways of 5 primed mice 7 days before intranasal OVA challenge. The dosages were 12 μg/ml (high), 1.2 μg/ml (intermediate) and 0.12 μg/ml (low). The effect of LAM on airway eosinophilia was determined by BAL. Again, PBS was administered intranasally to 5 primed mice as a control.

Results and Discussion

Figures 1 to 6 show the results of these experiments. Figures 1 and 2 show the number of cells recovered per ml and in total. Figures 3, 5 and 6 show that immunisation with high dose LAM gives rise to a reduction in eosinophil numbers equal to or greater than the reduction seen with whole live or dead BCG. This implies that LAM may be the active component in BCG that suppresses airway eosinophilia. Figure 4 shows that the number of macrophages in mice immunised with whole BCG (live or dead) is equivalent to the number found in mice immunised with high doses of LAM. This is supportive of a finding that TNF-α (which activates macrophages) is stimulated by LAM.

SECTION C2

Materials and Methods

The OVA induced airway eosinophilia mouse model of atopic airway inflammation described in section C1 was used, together with a CD1 Knock-Out (KO) mouse model. The CD1 KO mice used were bred in turn from CD1 KO mice, prepared as described by Chen *et al.*, *Immunity*, 6:459-467 (1997), and confirmed as having CD1 KO status by standard techniques. Briefly, these involved FACS staining of the mice as follows:

Mice were tail bled and the cells spun down into a pellet. The cells were treated with ACK lysis buffer and then spun down into a pellet. The pellet was resuspended in FACS buffer (PBS + 2% foetal calf serum + 0.1% sodium azide). The cells were then stained with PE-anti-CD1d and analysed by flow cytometry to identify CD1 KO mice.

To establish a dose response curve for LAM, doses of 3.6 to 12 μg/ml of LAM obtained as in Section A and formulated as in Section B were administered intranasally to the airways of 5 OVA-primed mice 7 days prior to intranasal OVA challenge. PBS was administered intranasally to 5 primed mice as a control. The effect of LAM on airway eosinophilia was determined by BAL.

To establish the effect of LAM in CD1 KO mice, a dose of 12 μg/ml LAM obtained as in Section A and formulated as in Section B was administered intranasally to the airways of 5 CD1 KO mice 7 days prior to intranasal OVA challenge. PBS was administered intranasally to 5 CD1 KO mice as a control. The effect was determined by BAL.

Results

Figure 7 shows the effective dose of LAM with respect to a reduction in eosinophil numbers compared to a PBS control.

Figure 8 shows that immunisation with LAM gives rise to a reduction in eosinophil numbers in CD1 knockout mice. This shows that the LAM-induced reduction in eosinophil numbers is not dependent on the CD1 pathway, and the immune response is not CD1 restricted.

INDUSTRIAL APPLICATION

As will be appreciated from the above, the primary application of the invention is in anti-asthma treatment. That treatment may be prophylactic, to prevent or reduce the risk of non-asthmatics developing asthma, or therapeutic, to suppress established disease in an asthmatic.

The LAM-containing vaccines of the invention are formulated for respiratory administration, which will preferably involve the inhaled route for convenience. In turn, the presently preferred mode of administration will involve the use of a dispensing device, of which a container of LAM vaccine forms a part. That device can be a nebuliser, particularly a jet nebuliser such as that known as the Omron CX (Omron Healthcare, Singapore), the Medic Aid Ventstream or the Wright nebuliser (Aerosol Medicals, Colchester, UK) (where the vaccine is to be administered as an aerosol) or a dry powder inhalation device (such as the devices known as the Accuhaler and Diskhaler (Glaxo Wellcome)).

Respiratorially administered LAM has shown significant efficacy in reducing eosinophil numbers and in turn in reducing bronchial inflammation. The implications of this in both resisting the onset, and reducing the severity, of an asthma episode, and in treating non-asthmatics against developing asthma will be apparent to those skilled in this art.

Having described preferred methods of putting the invention into effect, it will be appreciated that modifications can be effected and yet still come within the general concept of the invention. It is to be understood that all such modifications are intended to be included within the scope of the present invention.

CLAIMS

1. A vaccine for inducing an immune response in a patient effective in the prophylactic treatment against, or therapeutic treatment of, asthma which comprises, as active agent, immunogenic lipoarabinomannan (LAM) formulated for respiratory administration to said patient.

2. A vaccine as claimed in claim 1 wherein the immune response induced is not, or not predominantly, a CD1 mediated immune response.

3. A vaccine for reducing the severity of asthma comprising an immunologically effective amount of immunogenic LAM formulated for respiratory administration.

4. A vaccine for reducing the risk of developing asthma comprising an immunologically effective amount of immunogenic LAM formulated for respiratory administration.

5. A vaccine according to any one of claims 1 to 4 in which said immunogenic LAM is isolated from a mycobacterium.

6. A vaccine according to claim 5 in which said immunogenic LAM is isolated from an *M. bovis* organism.

7. A vaccine according to claim 6 in which said *M. bovis* organism is *M. bovis* strain AN5.

8. A vaccine according to any one of claims 1 to 7 in which said immunogenic LAM is free of bacterial nucleic acid.

9. A vaccine according to any one of claims 1-4 wherein said LAM contains, as its saccharide component, from 27% to 52% mannose and from 73% to 48% arabinose.

10. A vaccine according to any one of claims 1-4 wherein said LAM contains, as its saccharide component, from 40% to 50% mannose and from 60% to 50% arabinose.

11. A vaccine according to any one of claims 1-4 wherein said LAM contains, as its saccharide component, approximately 45% mannose and approximately 55% arabinose.

12. A vaccine according to any one of the preceding claims in which said immunogenic LAM is a fluid.

13. A vaccine according to any one of the preceding claims which further comprises a respiratorially acceptable adjuvant.

14. A vaccine according to any preceding claim which further comprises a secondary immunogen selected from one or more Th1 type immune response inducing substances.

15. A vaccine according to claim 14 in which *Mycobacterium bovis* (Bacillus Calmette-Guerin) is included as said Th1 type immune response inducing substance.

16. A method of prophylactically treating a non-asthmatic patient against asthma which comprises the step of inducing an immune response in said patient by respiratorially administering an effective amount of immunogenic LAM.

17. A method of therapeutically treating asthma in a patient which comprises the step of inducing an immune response in said patient by respiratorially administering an effective amount of immunogenic LAM.

18. A method according to claim 16 or 17 in which the immune response induced is not, or not predominantly, a CD1 restricted immune response.

19. A method according to any one of claims 16-18 in which said immunogenic LAM is administered in the form of a vaccine as claimed in any one of claims 1 to 15.

20. A method according to any one of claims 16-19 in which said immunogenic LAM is administered by inhalation through the mouth of said patient.

21. A method according to any one of claims 16-19 in which said immunogenic LAM is administered intranasally to said patient.

22. The use of immunogenic LAM in the preparation of a medicament for the therapeutic treatment of asthma.

23. The use of immunogenic LAM in the preparation of a medicament for prophylactically treating a non-asthmatic against developing asthma.

24. Use according to claim 22 or 23 in which said immunogenic LAM is isolated from a mycobacterium.

25. Use according to claim 24 in which said mycobacterium is an *M. bovis* organism.

26. Use according to claim 25 in which said *M. bovis* organism is *M. bovis* strain AN5.

27. Use according to any one of claims 22 to 26 in which said immunogenic LAM is free of bacterial nucleic acid.

28. Use according to claim 22 wherein said immunogenic LAM contains, as its saccharide component, from 27% to 52% mannose and from 73% to 48% arabinose.

29. Use according to claim 22 wherein said immunogenic LAM contains, as its saccharide component, from 40% to 50% mannose and from 60% to 50% arabinose.

30. Use according to claim 22 wherein said immunogenic LAM contains, as its saccharide component, approximately 45% mannose and approximately 55% arabinose.

31. Use according to any one of claims 22-30 wherein in preparing said medicament said immunogenic LAM is combined with a respiratorially acceptable adjuvant such that the medicament is formulated for respiratory administration.

32. A device for prophylactically or therapeutically treating asthma which includes a container from which a vaccine according to any one of claims 1-15 is dispensable to the airways of a patient in need of such treatment.

33. A device according to claim 32 from which said vaccine is dispensable by inhalation through the mouth of a patient.

34. A device according to claim 32 from which said vaccine is intranasally dispensable.

Figure 1

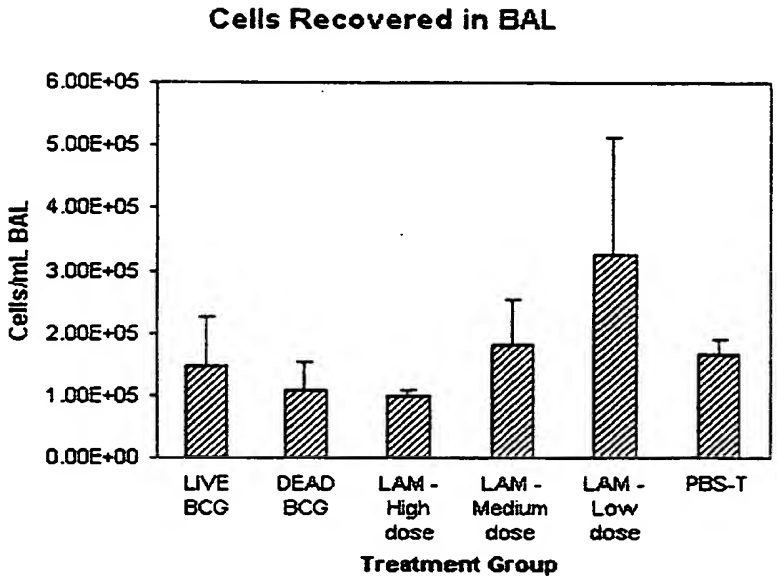


Figure 2

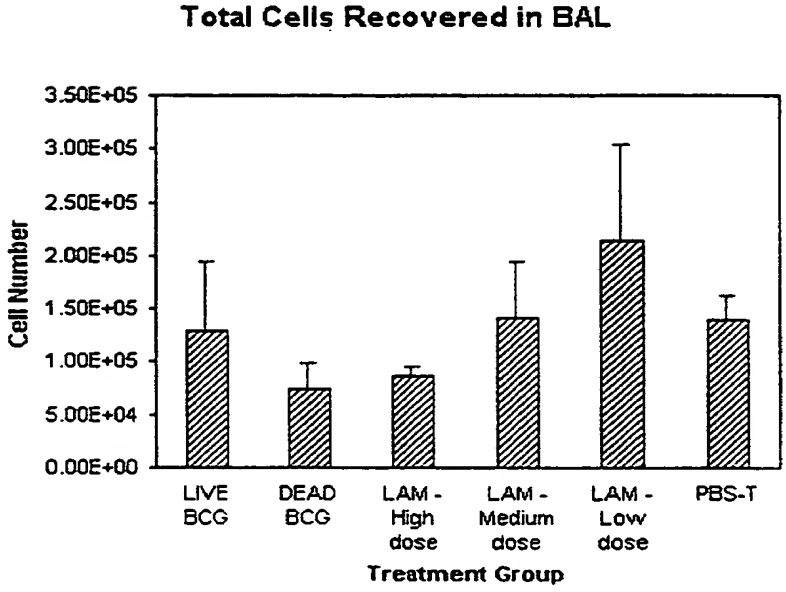


Figure 3

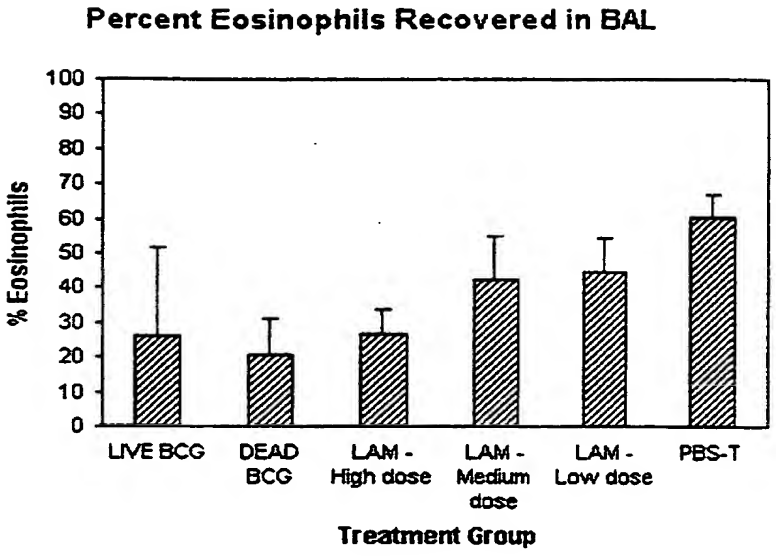


Figure 4

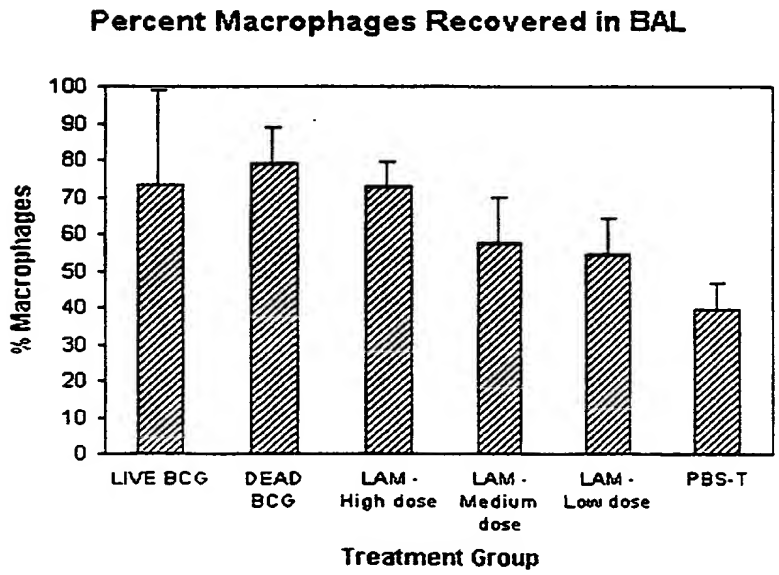


Figure 5

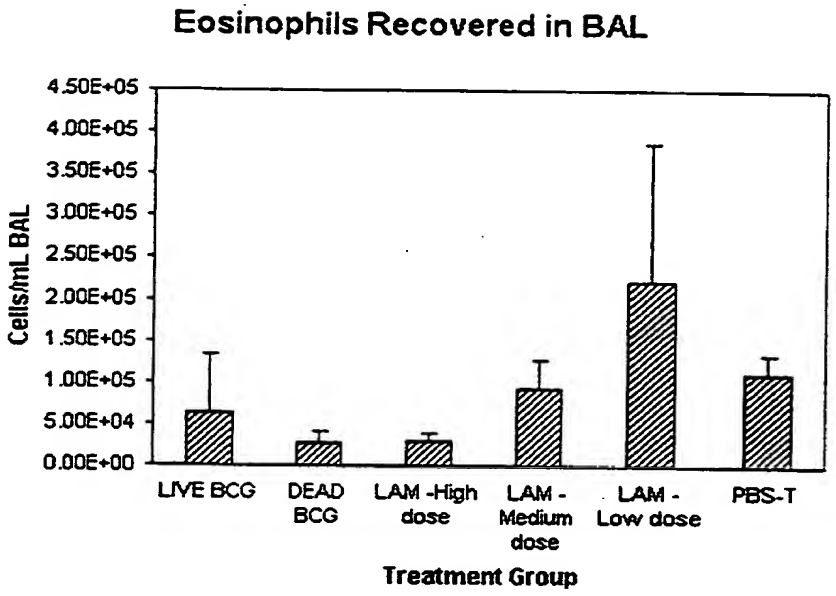


Figure 6

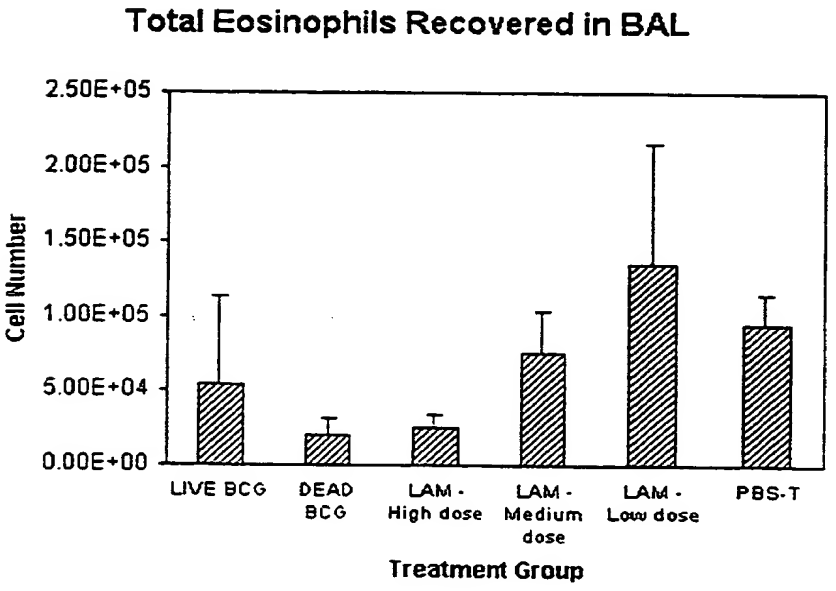


Figure 7

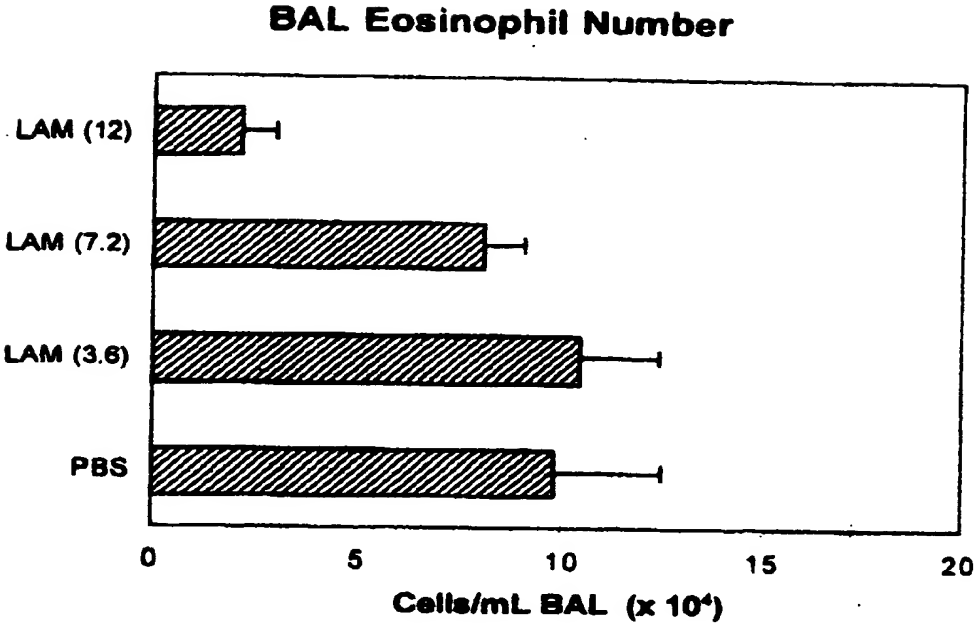
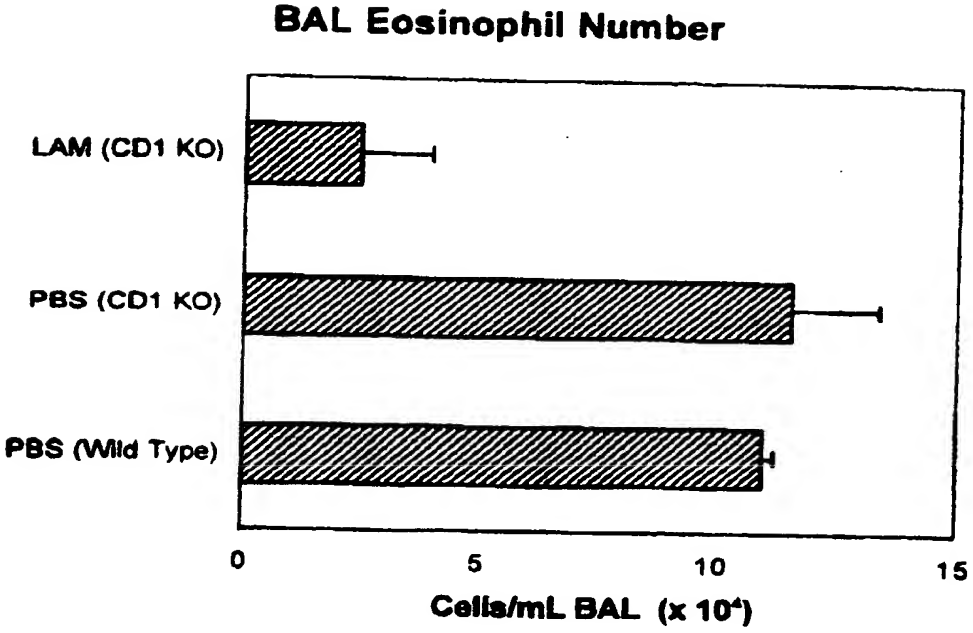

BAL Eosinophil Number
LAM (12)
LAM (7.2)
LAM (3.6)
PBS
0
5
10
15
20
Cells/mL BAL (x 10⁴)

Figure 8


BAL Eosinophil Number
LAM (CD1 KO)
PBS (CD1 KO)
PBS (Wild Type)
0
5
10
15
Cells/mL BAL (x 10⁴)

INTERNATIONAL PRELIM[redacted]RY EXAMINATION REPORT

[redacted]ernational application No.
PCT/NZ00/00027

I. Basis f the rep rt

1. With regard to the **elements** of the international application:*

[X] the international application as originally filed.

[ ] the description, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the claims, pages , as originally filed,
pages , as amended (together with any statement) under Article 19,
pages , filed with the demand,
pages , received on with the letter of

[ ] the drawings, pages , as originally filed,
pages , filed with the demand,
pages , received on with the letter of

[ ] the sequence listing part of the description:
pages , as originally filed
pages , filed with the demand
pages , received on with the letter of

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, was on the basis of the sequence listing:

[ ] contained in the international application in written form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

4. [ ] The amendments have resulted in the cancellation of:

[ ] the description, pages

[ ] the claims, Nos.

[ ] the drawings, sheets/fig.

5. [ ] This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* *Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*

** *Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report*

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims **1-34**	**YES**
	Claims	**NO**
Inventive step (IS)	Claims **1-34**	**YES**
	Claims	**NO**
Industrial applicability (IA)	Claims **1-34**	**YES**
	Claims	**NO**

2. Citations and explanations (Rule 70.7)

Novelty (N) and Inventive Step(IS)

The citations in the International Search Report, namely

(i) Lawn, S.D.et al "Evaluation of a commercial immunodiagnostic kit including lipoarabinomannan in the serodiagnosis of pulmonary tuberculosis in Ghana." Tropical Medicine and International Health, Vol. 2, No. 10, Oct 1997, pages 978-981 and

(ii) Erb, K.J. et al, "Infection of Mice with Mycobacterium bovis - Bacillus Clamette-Guerin (BCG) suppresses allergen-induced airway eosinophilia." J. of Experimental Medicine, Vol. 187, No. 4, 1998, pages 561-569

do not disclose the lipoarabinomannan vaccine formulated for respiratory administration.

In Erb, Mycobacterium bovis is disclosed for treating asthma. Although Mycobacterium bovis produces lipoarabinomannan (see Lawn S.D. page 979, lines 4 to 5.), there would appear to be an inventive step in formulating a vaccine using this component.

Industrial Applicability (IA)

Industrial Applicability is not in doubt.

Rule 67 lists the subject matter which under Article 34(4)(a)(i) an international preliminary examination is not required to be carried out. At item (iv) it specifies methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods, as such matter. However the agreement between WIPO and Australia further qualifies this by excepting from exclusion any subject matter which is examined under national grant procedures. Claims 16-21 have nonetheless been considered because the identified subject matter does not contravene Australian law.